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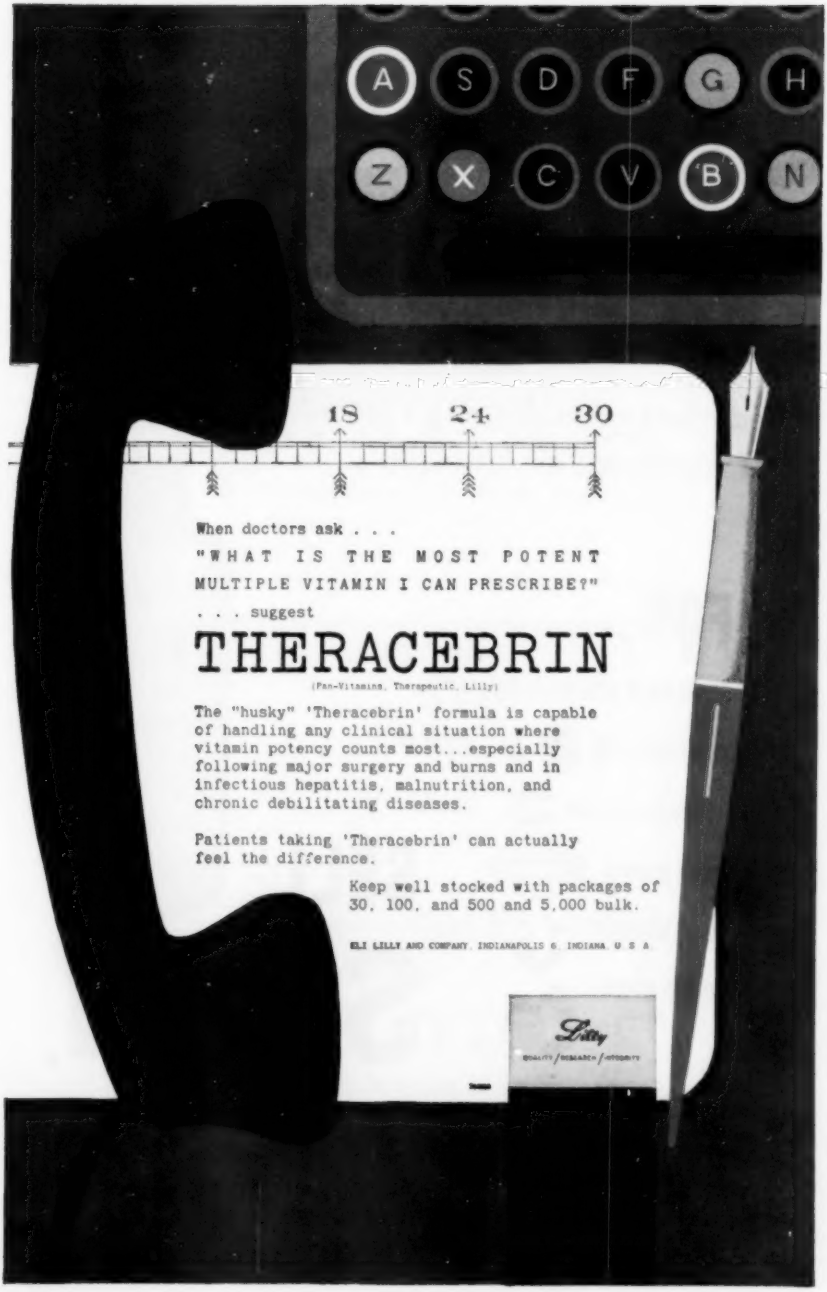
American Journal of Pharmacy

Published monthly by the Philadelphia College of Pharmacy and Science
43d Street, Kingsessing and Woodland Avenues, Philadelphia 4, Pa.

Annual Subscription $4.00 — Foreign Postage, 25 Cents Extra
Single Numbers, 40 Cents — Back Numbers, 50 Cents

Second Class Postage Paid at Philadelphia, Pa.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EDITORIAL

SEGREGATED BLOOD

IT seems impossible to believe that, in a nation as enlightened as we Americans presume ours to be, a law could be passed in one state requiring blood from colored and white donors to be strictly segregated and used only in the respective racial category.

It is well known that blood from all human beings, regardless of skin pigmentation or ethnic origin of the donor, cannot be differentiated by any known test. While it is true that different races have a different percentage distribution of blood types, all types are found among all races and no known method can be used to ascertain the origin of a given sample. It also seems quite well established that the transfusion of blood from one person to another does not convey any potential change in racial characteristics nor does it change the genetic pool of the recipient. While it is true that some Russian geneticists claim that the transfusion of blood from one animal to another can alter certain of the recipient's characteristics, these results are looked upon with great skepticism by other scientists.

During the war, blood from Negroes was transfused into whites and *vice versa* thousands of times without any observable change, then or later, in either group. The truth is that there is nothing about the Negro other than skin pigmentation which makes him different from a white person in spite of the alleged inferiority of the Negro as claimed by certain people in the South. It is, of course, true that—after generations of an existence with an underprivileged status, with separate and *unequal* educational facilities, poor nutrition, poor housing, and little or no opportunity—Negroes quite often do bear the stigma of such oppression. There is, however, not the slightest bit of scientific evidence that they are biologically inferior to other persons and no reason to believe that equal treatment would not result after just a few generations in full equality in every sense of the word. It is quite easy to show how certain white people with the highest social pedigree have, through several generations of inbreeding, produced *really* inferior biological specimens. Yet, some of these same speci-

mens have in recent times been looked upon as an aristocracy, set apart from ordinary man in both their prestige and privilege.

It is somewhat ironic that we in the United States presume to pose as world leaders when the vast majority of the earth's people are not white. Within our own country, we make only feeble attempts to establish that we truly believe in the dignity of all men and their biological oneness. The recent law to which we refer concerning segregated blood is but one of a long series of acts which are based on ignorance, narrow-mindedness, and prejudice. It is small wonder that we face mounting difficulties in our efforts to have the peoples of the world look to us for guidance and, unless we change our own basic philosophy, we shall fail. Only a fool would believe someone who professes a philosophy which he abhors at home and fails to live by. In Asia and Africa, as well as with the Negroes in our own country, we are not dealing with fools but with intelligent human beings, each with a touch of the Divine which makes all men seek and even die for the recognition and respect which is their God-given right.

L. F. Tice

PILZATROPINE, THE AMBIGUOUS ALKALOID

By Varro E. Tyler, Jr.*

NO other plant is surrounded by a lore as curious and as contradictory as that associated with *Amanita muscaria* (Fr.) S. F. Gray. As early as the 13th century Albertus Magnus wrote in *De Vegetabilis* of its use as a fly killer, especially when pieces of it were soaked in milk. For 700 years it was assumed that this activity was responsible for the common name of the fungus, fly agaric or bug agaric. Oddly enough, the ability of the mushroom to kill flies has never been confirmed scientifically.

Explorers and travelers who toured Siberia, beginning in the early part of the 18th century, have repeatedly confirmed the use of the fly agaric as a narcotic or intoxicant by the Koryak and neighboring tribes of Kamchatka. J. Ramsbottom (1) lists these authors and quotes a vivid description of an orgy resulting from this use of the plant. The effects described are reminiscent of those caused by the Solanaceous narcotics used by various natives of the western hemisphere (2).

It has also been asserted that ingestion of the mushroom was responsible for the so-called Berserk-fury of the Viking period, but P. Thorsen (3) has reviewed the literature on this topic and concludes that such a postulation is unfounded.

The intoxicating effects of this mushroom have prompted a reevaluation of its common name by V. P. and R. G. Wasson (4). These authors conclude that the appellation "fly" or "bug" was originally descriptive of the temporary demented condition produced by the plant, rather than being derived from its doubtful toxicity toward flies.

Attempts to isolate the active toxic principle(s) of the fly agaric began nearly 150 years ago, and were apparently culminated successfully in 1869 when O. Schmiedeberg and R. Koppe (5) obtained a syrupy base which they named muscarine. Determination of the structure of this quaternary ammonium compound proved to be a particularly knotty problem and of sufficient difficulty to attract the interest of scores of chemists down to the present day. An excellent review of this intriguing problem has appeared recently (6). The physiological activity of muscarine was ascertained more easily,

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and it was shown to produce, among other effects, a stoppage in diastole of the isolated frog heart.

E. Petri, in a dissertation prepared in 1880 under the direction of B. Luchsinger (7), asserted that there was a limiting factor in the dosage of muscarine required to effect this cardiac arrest, and that when a dose exceeded this limit, the activity of the heart was accelerated instead of being arrested. Since these results contradicted his own, Schmiedeberg immediately undertook an examination of an identical sample of the commercial muscarine which Petri had used and which had been prepared from *A. muscaria* by Gehe and Co. in Dresden.

In his published report of this study, Schmiedeberg (8) concluded that the product contained, in addition to muscarine and choline, a rather significant quantity of a base which was responsible for neutralizing the cardiac-arresting activity of the muscarine, thus acting in the same way as atropine. This base was obtained from the commercial muscarine by rendering it alkaline and extracting with ether. On evaporating the solvent an alkaline mass remained which, like atropine, could be converted to a crystalline hydrochloride or a less clearly crystalline sulfate. Because of the small quantity available, it was not possible to establish physical constants for the alkaloid, but it was shown to be the agent responsible for the physiological actions reported by Petri. It could not be ascertained if the base was a new alkaloid which occurred in the fly agaric in certain cases, or if it was an artifact formed from other basic compounds during the preparation of muscarine, or if it was an accidental adulteration with one of the known Solanaceous alkaloids.

Schmiedeberg neglected to assign a name to the compound, but this deficiency was remedied by R. Kobert (9, 10) in 1891. He reported that the fly agaric examined by him contained, in addition to choline and muscarine, a third active principle. The properties of this compound were antagonistic to muscarine, dilating the constricted pupil, accelerating the slowed heart, and finally being excreted unchanged in the urine. These activities, which were the same as those of the compound isolated by Schmiedeberg, prompted Kobert to title the principle, "pilzatropine" or alternatively, "muscaridine".

Both of these names have remained in use in the literature. Pilzatropine is perhaps more common, but muscaridine is widely used by German authors. Some writers have felt compelled to translate the prefix, pilz-, into other languages. Thus Ramsbottom (11), an

Englishman, refers to myceto-atropine, and H. Romagnesi (12), writing in French, employs the term mycoatropine.

Kobert further postulated that it was the presence of this compound which produced the narcotic effects of the fungus described by early travelers in Siberia. He also believed that the presence in the fly agaric of these naturally antagonistic compounds, muscarine and pilzatropine, accounted in certain instances for the reports of the mushroom having been eaten with impunity. Finally, he was able to establish the presence of choline, muscarine and pilzatropine in another mushroom, *Russula emetica.*

About this same time, Y. Inoko (13) reported that the panther fungus (*Amanita pantherina* (Fr.) Quelet) enjoyed a high reputation as a fly killer in Japan and added that its toxic properties were considerably greater than those of *A. muscaria.* He subsequently demonstrated the presence of an atropine-like principle in the panther fungus (14) which was accompanied by choline and muscarine. An atropine-like activity was also found in an unidentified species of *Collybia.*

In 1903, E. Harmsen (15) isolated muscarine from a quantity of *A. muscaria* collected in Bavaria. The crude muscarine was made alkaline and extracted with ether but failed to yield an atropine-like compound as determined by pharmacological tests on the frog heart and eye of the cat. Harmsen emphasized that this should not be taken to mean that pilzatropine never occurs in the fly agaric, but rather that the occurrence of the substance might be influenced markedly by developmental and environmental factors.

The next attempt to isolate an alkaloid from *A. muscaria* was made by J. Honda in 1911 (16). A diluted alcoholic extract of the dried, powdered fungus was purified with lead acetate and the alkaloids precipitated with phosphotungstic acid. After decomposition of the preciptate and subsequent purification, a bright yellow, gummy mass was obtained which finally yielded a crystalline hydrochloride. From this, two bases were separated on the basis of the differential solubility of their platinum salts and were named α- and β-myketosine. The quantity obtained was not sufficient to allow determination of their chemical and physical properties. Physiological tests carried out on frogs and rabbits revealed that both compounds possessed hypnotic activity, but only in relatively large doses. Honda did not speculate on the relationship of α- and β-myketosine to pilzatropine.

More than 40 years passed before V. Kwasniewski (17) undertook a re-examination of the pilzatropine problem in 1954. A quantity

of the dried, powdered mushroom was extracted with 95% methanol, and after purification with lead acetate, the bases were precipitated with Mayer's reagent. The preciptate was decomposed and the resulting residue dissolved in ether and then transferred to 0.1 *N* sulfuric acid. This solution was evaporated, and the residue taken up in distilled water. Two drops of this solution failed to dilate the pupil of the human eye, and it was concluded that pilzatropine was not present in the mushrooms investigated.

The most recent contribution to our knowledge of pilzatropine was made in 1955 when B. Lewis (18) reported the isolation of compounds from *A. muscaria* and *A. pantherina* which were not distinguishable from *l*-hyoscyamine on the basis of the tests performed. One kg. of fresh material of each of these species was collected in the vicinity of Cape Town, South Africa. After drying, the plant material was extracted with 95% ethanol, the extract concentrated and purified by partition between chloroform and 1% hydrochloric acid. The residue from *A. muscaria* yielded 1.1 mg. of crystalline material; from *A. pantherina*, 1.8 mg. The melting point of the crystals and their aurichlorides, *Rf* values, Vitali's tests and bioassays (rabbit eye dilation) all corresponded to the values or responses obtained with *l*-hyoscyamine. Lewis concluded that while it is not possible to ignore the occurrence of geographical variation in alkaloid content of mushrooms, it appears that Kobert's pilzatropine is in fact *l*-hyoscyamine, and that the neurological signs due to poisoning by mushrooms of the species studied are due to this alkaloid.

It would be convenient if a review of the subject of pilzatropine could end here, but if it did, the alkaloid could not properly be labeled ambiguous. Two additional types of evidence must be considered before a critical evaluation can be complete.

The first of these came to light in 1953 when T. Wieland and W. Motzel (19), in examining the nature of a compound previously isolated from *Amanita mappa* which had been designated "mappin", concluded that the compound was actually bufotenine. This alkaloid had originally been isolated by C. Phisalix and G. Bertrand (20) from the secretion of the parotid gland of the common European toad (*Bufo vulgaris* Laur.). Wieland and Motzel were quick to recognize the intriguing nature of the occurrence of the same unusual compound in both "toads" and "toadstools", but at the present this can only be attributed to coincidental nomenclature. Since bufotenine may be detected easily by chromatography, the authors reviewed its occcur-

rence in fungi and established its presence in *A. pantherina* and in small quantities in *A. muscaria.*

It has since been established (21) that bufotenine has a definite hallucinogenic activity in man, at least when injected intravenously, and it has been proposed that this compound may be responsible for the intoxicating effect of the fly agaric as employed by the Siberian natives (22). If true, this would apparently eliminate the necessity of hypothesizing a pilzatropine to explain such activities.

The second type of evidence which casts some doubts upon the assumption that the pilzatropine problem has been completely solved lies in the results of extensive observations on the influence of climate on the active principles of medicinal plants.

The response of plants to environmental factors is extremely complex, but it is possible to draw one general conclusion: a plant produces a maximal content of active principles under those climatic conditions which allow the optimum development of the plant itself. Although active principles may respond to climatic factors both qualitatively and quantitatively, the qualitative reaction (total absence of a certain principle or group of principles) has not been established with certainty up to the present (23). While it is entirely possible on theoretical grounds that a total lack of formation of a chemical substance could result from too low or too high an intensity of some climatic factor, this is not a common condition and illustrations in the literature are not numerous. Environment would be much more likely to cause fluctuations in the quantity of pilzatropine present in *A. muscaria* or *A. pantherina* than it would be to cause a total absence of this constituent.

The most important factors that affect the content and the composition of the active principles in plants are not climatic but genetic. Here again variations in the quantity of an active material are much more common than qualitative variations. For example, the alkaloid content of ergot has been shown to range from negligible up to as high as 1%, but M. Pöhm (24) asserts that he was never able to find an entirely alkaloid-free ergot. It seems doubtful that the variations which have been reported in the pilzatropine content of *A. muscaria* could be accounted for entirely on the basis of either climatic or genetic factors.

The final chapter of the story of this ambiguous alkaloid remains to be written.

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GUARDIANSHIP *

By W. Paul Briggs **

MY only qualification to address this NABP-AACP meeting is my selfish desire to visit again with my good friends of the South. I am a former retail pharmacist and an ex-college professor, but my only experience with a Board of Pharmacy occurred years ago when I slipped by the District of Columbia Board and acquired my license as a pharmacist.

You are guardians, not only of the public health, but sponsors and guardians of the practitioners of pharmacy. In a professional sense, pharmacists are wards of their college and their state Board of Pharmacy. Your guardianship responsibility never ends. I have two questions to ask Boards and colleges as they strive to meet their guardianship responsibilities.

You received the neophyte, you trained him, you examined him, and finally you blessed him with the power of a sovereign state. Now he is a member of the profession—he has reached his goal—he is a licensed pharmacist. But have we done everything possible to enrich him with the ideals and dignity of pharmacy? Of equal importance, do we follow up, throughout his professional lifetime, to insure both his contentment and competence as a pharmacist?

Our training centers, in the distant past, were often mere technical schools, serving a practical means to the end of registration. Our Boards, many years ago, functioned largely as policemen. Both schools and Boards felt their job was finished when the state issued a license to practice pharmacy. Today, our strong colleges of pharmacy provide sound education for broad professional service and preparation for enjoyment of a full and useful life. And our Boards have assumed professional leadership responsibilities in addition to their statutory duties. Colleges and Boards of Pharmacy have come of age.

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* Presented at District No. 3 NABP-AACP Meeting, Biloxi, Mississippi, August 25, 1958.

** Executive Director, American Foundation for Pharmaceutical Education.

College faculties have a few years in which to train young men and women to be good pharmacists and good citizens, and bring them up to graduation. Our Boards have a few days to examine applicants and pass upon their qualifications for registration as pharmacists. But college graduation and Board registration do not end your professional responsibilities. Indeed, if pharmacy is to achieve its potential, these events only mark the beginning of your moral obligation as guardians of the profession.

Several weeks after taking my examination for registration, I received a crudely typed postal card directing me to come to the Secretary of the Board to receive my Certificate. I had worked toward this goal for many years. At that time, I wanted my Board Certificate more than anything else in the world.

The Secretary was a charming gentleman but he operated one of the most unsightly drug stores I have ever known. And it was located in the heart of our dreariest slum. When I finally climbed over discarded boxes and dirty displays and got to the back of the store, I recognized the Secretary, even in the semi-darkness of his uninviting shop. He greeted me warmly, handed me the rolled-up Certificate, and returned to serve his customer buying, as I remember, chewing tobacco and turpentine. I thanked the Secretary and left—a thoroughly disenchanted young man.

I am not sure just what I had expected, but I clearly remember that my youthful enthusiasm for pharmacy was temporarily depressed by this dreary experience. I know that other Boards of Pharmacy, even then, were not so indifferent. And I am sure that all Boards today are striving to meet every responsibility of their important assignments in the most effective manner.

Then why do I relate this unhappy incident of thirty years ago? Because I have long carried the feeling that we have failed to fuily embrace our opportunities to impress our new colleagues and the public with the importance and dignity of pharmacy.

Every time a Board of Pharmacy issues a new license, we have a golden opportunity to impress the public and strengthen the moral fibre of pharmacists. Now my first question. Why don't we capitalize on this unique opportunity by conducting public Board of Pharmacy registration ceremonies in every state?

Perhaps some Boards do this now. The New Jersey Board, for at least a few years, held public registration services until World

War II forced discontinuance. I know there will be real difficulties involved in arranging formal ceremonies for this purpose. But I believe the potential benefits in upgrading pharmaceutical morale and enhancing public esteem for pharmacy would make the effort worthwhile.

I hope that someday soon pharmacists in every state will be inducted into the profession at public ceremonies, conducted by the Boards, in a manner similar to college graduation. I should think governors, mayors, state legislators and other state officials would welcome an opportunity to address newly registered pharmacists, their families and friends, at a Board of Pharmacy convocation.

If the office of the Board is not strategically located, it should be possible for some members of the Board to journey to a point convenient to the highest concentration of newly licensed pharmacists. College faculties and state association officials would want to attend this important public function. Surely all the other health professions would send local representatives on such an occasion.

You have some mighty big states down here, and it is unlikely every new licensee could attend the principal ceremonies even when centrally located. But you also have well-organized county groups. Neighboring counties might join together to provide a suitable meeting for Certificate presentations to new pharmacists living in remote sections of the state. Here, civic officials or state legislators from these sections, with local representatives of the Board, colleges, the state association and the other health professions, could make these area services quite impressive. Everything is relative—the number of new pharmacists and the size of the audience would not be important. But the occasion itself and the recognition from colleagues and the public would long be remembered by our new members. There will be many details to resolve—some troublesome, some difficult—but none insurmountable, and, in my view, well worth a good trial.

Now, what could we hope to achieve from a nation-wide program of this general type?

I believe every pharmacist, receiving his license at an appropriate public ceremony, would be impressed with his status as a member of the health sciences team and with the importance and dignity of his new profession. I believe he would gain a better appreciation of his place in society. He would feel wanted and accepted. He would enjoy greater self-respect and this would favorably influence his daily

conduct as a practicing pharmacist. I think he would start his career proud of pharmacy and determined to observe the laws and codes of ethics governing the profession. The presentation services might well include public acknowledgment of the A.Ph.A. Code of Ethics. I think that a well-developed program of formal admission to the profession might be effective in lowering the level of pharmaceutical frustration, and raising the level of pharmaceutical morale.

Surely the public would be impressed by a formal licensing ceremony conducted by the Board. Participation of civic officials would certainly give new meaning to the importance of the drug store. Local newspapers would provide good—and free—publicity for pharmacy. It would be hard to find a better forum from which to tell the story of pharmacy to the public.

We are constantly talking about and seeking better public relations. Pharmacist registration ceremonies, in 49 states, conducted with the dignity and drama of college graduation, and effectively publicized, would have a favorable impact upon the public that could not be purchased at any price. And the opportunities to develop student recruitment campaigns around these public ceremonies would be highly productive. Moreover, the inherent total values to all of pharmacy might, in time, attract modest financial aid to insure the success of these state programs.

Is this just "the stuff as dreams are made on"? I do not think so. I am confident we could advance our cause by treating the right to practice pharmacy as important to us, and worthy of appropriate public recognition. I believe we owe at least this much to every new member joining our ranks.

My second question is directed primarily to teachers. It concerns your obligation to offer professional stimulation and educational refreshment throughout the lifetime of those you have trained. The question—Are we using every means at our disposal to help pharmacists help themselves?

In a recent report the AACP Committee on Future Enrollment Problems stated that 24% of pharmacy students in the twelve colleges studied, felt that "declining professionalism" and "declining prestige" constitute disadvantages of pharmacy as a career. In a survey of 9,000 U. S. college graduates in 1952, *Time Magazine* reported that, of the pharmacists questioned, 33% wished they had chosen some other field of life work. It should be noted however, that some

graduates in *every* field, from agriculture to zoology, also wished they had pursued other studies in college. It is probably unnecessary to add that drug stores are losing traditional business opportunities because they are not fully prepared for the violent battle for the dollar on Main Street.

I am not especially disturbed by these findings, except that they point up the need for college guardianship long after granting a diploma. Specifically, I feel that it is incumbent upon colleges to substantially extend their services to the practitioners of pharmacy. Many colleges have been offering refresher courses and extension services for sometime, and some treat this work as comparable in importance to their classroom instruction. But the tempo of modern drug research and the merchandising revolution are daily increasing the need for more frequent and more realistic retraining for the protection of the public and the preservation of the practice of pharmacy in every state.

I hope we can soon persuade pharmacists themselves that they need retraining for their own security and success. I know that some colleges have met with disappointment in the lack of interest in such programs from the very men they sought to help. The very best refresher course or extension service, offered by any college, is doomed to failure unless pharmacists will receive it. But I believe pharmacists are becoming aware of their inevitable obsolescence in the absence of periodic training throughout their career. As more colleges offer progressive refresher programs, and as the results, however small at first, provide hard-cash values, acceptance of this form of college guardianship will increase. This will help to halt any "decline in professionalism and prestige", provide better pharmaceutical services for the public, and reduce the level of discontent and frustration among pharmacists.

I know it is not easy for colleges to find the time, instructors, audience or money to offer formal refresher or extension courses. But the urgent need by pharmacists, and our guardianship responsibility, make it imperative that we join forces to develop some form of continuing education in every state. When we cannot do this job just as it should be done, let's at least make a start. The best way to begin any task is to start. In the words of Teddy Roosevelt, "Do the best we can, with what we have, where we are."

Where we cannot provide regular refresher courses at the college, or formal, state-wide, college-sponsored extension courses, why can't we arrange for informal local retraining programs on a cooperative basis? "Informal refreshers" might be short of ideal, but we are morally obligated to attempt to bring some professional stimulation to every pharmacist to fulfill our guardianship responsibilities.

Could the faculties of our colleges, knowing the pharmacists of their state, draft a workable Instruction Manual, outlining subject matter and procedure, to guide non-academic leaders in organizing a "local" refresher course? Could local meetings be held at various convenient centers throughout the state? At some meetings, perhaps a member of the college staff could serve as coordinator, as well as an instructor. At other meetings perhaps the duty of coordinator could be assumed by an officer of the state association or by a member of the Board living in the area, or by an official of the county association.

Could we organize a local instruction staff that might be supplemented by traveling wholesale drug representatives and pharmaceutical manufacturers' detail men working throughout the state? These are usually well-informed men, eager to serve pharmacy in every possible way. I think they would be glad to serve, and I know they could bring useful information to local refresher sessions. Following the college prepared Instruction Manual, local pharmacist leaders, plus available, but hidden talent, and, of course, a college faculty member whenever possible, could stage worthwhile business and professional classes.

What would we use for text books? We have an abundance of up-to-date material on professional and merchandising developments in pharmacy that is available from wholesalers and manufacturers for the asking. Round-table discussion of surveys, reports and feature articles from the alert drug press could be highly productive. But most of us need some stimulus to make us submit our intellectual batteries to recharging. This is a basic objective of a "local" seminar. I believe, as an emergency substitute for college refresher and extension courses, "local" refresher meetings would be a real step forward. And we could do this almost without cost. We should not expect our first efforts with volunteer instructors to be perfect but, once a start has been made, we could then expect continuous progress toward quality retraining where it is most needed. These pharmaceutical

"Chautauqua" meetings would certainly provide incentive for learning and could contribute substantially to broadening the perspective and developing the professional and business competence of pharmacists.

Are colleges and Boards doing enough for pharmacy? Have we yet seized every opportunity to help pharmacists? I would not presume to give an answer to these questions. But I think pharmacy must answer them.

I have faith in the future of pharmacy—provided we do not just cry about our problems or expect solutions by divine decree. Possibly the two programs I have suggested, if soundly developed, would give us some worthwhile public relations and helpful stimulation for all pharmacists. Success in advancing the profession means hard work and alert use of every asset of pharmacy. And we must learn to dramatize and publicize every aspect of pharmaceutical service on every possible occasion. Our Boards and colleges are in strategic positions to do both, and thus contribute to developing better pharmacy and better public appreciation for pharmacy. The members of NABP-AACP District No. 3 might make real contributions to these ends by assuming leadership in developing public Board of Pharmacy registration ceremonies and realistic refresher programs to reach every pharmacist in every state of the deep South. Probably, in most instances, both programs would be more effective if *jointly sponsored* by the state Boards of Pharmacy and the colleges of pharmacy.

We will never be content with our place in the world of the health sciences, or our community, until every pharmacist gives more to the profession than he tries to take. Let's not stop when our primary job is done—let's do a little extra. This is how great advances are made.

LIMITATIONS IN THE CHEMICAL TREATMENT OF 5461 CASES OF HODGKIN'S DISEASE

By John R. Sampey *

AN earlier study showed that nitrogen mustards and TEM were the most frequently employed chemicals in the management of Hodgkin's disease (21). In the present survey more than 4,000 patients have been given these two agents. Antibiotics, colchicines and ACTH/cortisone are the next most used chemicals in H. D. therapy. H. D. has not responded to the wide spectrum of chemotherapeutic agents noted in the management of the leukemias (22, 23). Table I summarizes the chemotherapeutic treatment of H. D. since 1949.

TABLE I

CHEMICAL TREATMENT OF 5461 CASES OF H. D.

Agents	No. of Refs.	No. of Cases	No. of Refs. Not Giving Remissions	No. of Remissions	Remission Rates
Nitrogen Mustards	215	3257	36	1420	65%
TEM	76	784	9	411	59%
Antibiotics	46	512	5	236	53%
ACTH/Cortisone	40	140	2	83	67%
Colchicines	23	144	2	86	81%
Miscellaneous	123	624	3	322	55%

A number of the clinical reports tabulated in this table fail to give the number of patients responding to the therapy (column 4). The remission rates were calculated (column 6) from reports publishing both the numbers treated and the numbers responding.

The limitations in the chemical treatment of H. D. are due not only to the incompleteness of the published reports, but to the lack of objective standards for the evaluation of the therapy, and to the toxic and other undesirable reactions of the chemicals. Some reports

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are supported by detailed data on both the clinical and hematologic picture of the patient before and after the therapy, while others give only the investigators general impressions of the treatments, or the patients' subjective reactions to the therapy. The limitations induced by the chemicals themselves will be indicated under each of the types of agents employed.

Nitrogen Mustards. Nitrogen mustards account for 60% of the cases in Table I. The remission rate of 65% is good, but 36 reports failed to give data on the number responding. The newer nitrogen mustards, CB 1348 and nitromin, have a higher remission rate than the older HN2 and HN3 compounds. Several reports emphasize the toxic reactions of mustards (16, 20), with Sanchez (24) reporting as high as 70% of his patients showing toxic manifestations. Videbaek (30) maintained that mustard therapy caused more discomfort and involved more risk than did irradiation. Mrazek (17) warned of bone marrow depression, and Piemonte (19) found two of 20 patients on HN2 died of aplastic anaemia due to the drug. Eisenstadt (7) noted a case of H. D. hastened by nitrogen mustards.

TEM. Nine of the 76 published studies on triethylene melamine therapy of H. D. failed to give the number of patients responding. Sawitzky (27) noted more toxic reactions in H. D. patients than in those with lymphosarcoma, and Bond (2) described marked toxic reactions in 3 and mild in 4 of 7 H. D. cases. Mrazek (17) reported serious bone marrow depression (BMD) in 1 of 11 H. D. patients on TEM alone, and 11 of 35 showed BMD who had received irradiation therapy previous to TEM. Ferrari (8) noted bone damage in 6 of 23 patients with lymphomas and leukemia.

Antibiotics. Antibiotics rank third in the number of H. D. patients treated, and there are no reports of serious side reactions. But the remission rate of 53% is the lowest of the widely used chemotherapeutic agents.

Colchicines. The colchicines also are remarkably free from undesirable side reactions in H. D. therapy, and the remission rate of 81% is the highest in Table I, but few investigators report complete remissions.

ACTH/Cortisone. These hormones rate second only to colchicines in the response shown in Table I, but the 40 published reports

contain many limitations to the therapy. Saric (26) and Marchal (15) reported a high incidence of terminal T. B. in H. D. patients receiving the hormones, and the latter noted the inconsistent results with each drug (12). Lesca (11) described the death of a patient due to exudative pleuropericarditis after cortisone and chloramine therapy, and Aubertin (1) noted severe diabetes followed ACTH therapy of H. D. Marchal (13) described hemorrhages like strokes following the use of ACTH. Boudin (3) ascribed intestinal perforations to cortisone therapy, and Justin-Besancon (10) described how large doses of cortisone were contraindicated in H. D.

Miscellaneous Agents. Myleran, P^{32}, phosphoramides, folic acid antagonists and urethan account for one-fourth of the 624 patients treated with miscellaneous chemicals. The remission rates range widely, from 77% for 53 cases of myleran to 14% for 34 on FAA, and 12% for 32 on urethan. Cifarelli (4) cited a case of H. D. that was contraindicated by urethan, and Winthrope (31) listed FAA and 6-MP therapy as contraindicated in H. D. Paolino (18) found $Na_2S_2O_3$ aggravated 2 cases of H. D., and Sykes (29) reported that 5 patients undergoing splenectomy had the course of the disease accelerated. Methyltestosterone (28) produced a severe reaction in H. D.

Acknowledgments. The original literature has been made available by the National Library of Medicine, and the libraries of Furman University and the Greenville General Hospital.

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THE IMMUNIZATION OF CHILDREN

By L. F. Tice

THE greatly lowered mortality rate of infants and young children can be traced to many factors. These include better prenatal care for mothers, improved nutrition, the adoption of more sanitary procedures including insect control, and prophylaxis against the more serious infectious diseases.

While at one time, it was a common practice to expose young children to such diseases as diphtheria and whooping cough (pertussis) without any prior immunization, this resulted in the loss by death of as many as half of all children, and few mothers managed to raise all children born to them. Such tragedy is no longer a necessary part of parenthood if modern concepts are followed.

Experience over the years with various biologicals has shown that most, if not all, of these infectious diseases can be prevented or so modified that they no longer are a threat to the young child. The exact timing of the prophylactic injections and the best product to use in each instance is still debated by some authorities, but all will agree on their value. In this article, the five diseases against which children can be given considerable protection are discussed. They are: persussis, diphtheria, tetanus, smallpox, and poliomyelitis. The regimen of immunization presently considered optimum is also outlined.

Pertussis

This disease, also known as whooping cough, is quite serious in the very young child and it causes many deaths among infants. For this reason, it is wise to start immunizing the child against it at a very early age. Many pediatricians recommend the initial injection of pertussis vaccine at only one or two months of age. The regular pertussis vaccine is probably not as effective as the alum precipitated vaccine in the very young infant. On the other hand, the alum precipitated may occasionally cause a sterile abscess. Even so, the alum precipitated is the preferred form. It is given in three doses of 0.5 ml. each separated by an interval of 3-4 weeks between doses. When the child is 18 months old and again just before entering school,

a booster dose is given. No further injections beyond this are recommended since exposure to the disease itself is believed to maintain the antibody titer and the older child may show a marked reaction to the vaccine. If a pertussis epidemic should break out and the older child is to be given a booster dose, the regular vaccine (not alum precipitated) should be used.

Diphtheria

While the need for the early immunization against diphtheria is not as great as in the case of pertussis, it still is a disease causing high mortality in some countries. The immunization of the young child is clearly indicated. In the young child, the use of diphtheria toxoid is not usually followed by a serious reaction but in older children and adults, great care must be taken. This is because the repeated contact with diphtheria organisms or even the toxoid over the years causes many older persons to become highly sensitive to it.

The dose of toxoid given a very young child for purposes of immunization is fairly standardized, it being about 0.5 ml. (25 Lf units). Three such doses are given 4-6 weeks apart. When using the alum precipitated toxoid, only two doses are needed. After about age 5, the dose used as a booster every 3 or 4 years should be only 0.1 ml. and, for children over 12, the booster dose should be only 0.02-0.04 ml. to avoid a possible severe reaction.

Tetanus

While not transmitted from person to person, tetanus is a very serious and often fatal disease which can result from a relatively minor wound or injury. Immunization against tetanus is so effective and serious reactions to the toxoid so rare that it is considered wise to begin the immunization process against it in infancy and with later booster doses extend the immunity throughout life.

It is claimed that an individual who has had the basic immunization (3 injections of 0.5 ml. toxoid) followed by two well-separated booster doses in later years maintains a high antitoxin titer in the blood for many years and probably for life.

Combined Diphtheria, Tetanus, and Pertussis Immunization

The modern approach in pediatrics is to use a single product to simultaneously immunize the child against diphtheria, tetanus, and pertussis. For many years, a single product has been obtainable

containing both diphtheria and tetanus toxoids. This has been further modified by the addition of pertussis vaccine. This combination is available both plain and with all three in alum precipitated form. The dose of the product is 0.5 ml. for 3 doses separated by an interval of 4-6 weeks.

Here, it should be mentioned that the toxoids can be adsorbed on aluminum hydroxide or alumnium phosphate rather than being alum precipitated. This gives a quite similar suspension. Different suppliers use one or more of these three approaches to give equally satisfactory preparations.

For adult use, a combination of diphtheria toxoid (1.5 Lf units) and tetanus toxoid (7.5 Lf units) is available. This product does not contain pertussis vaccine and the dose of diphtheria toxoid is small enough so that a severe reaction in the adult is not likely. At this low level of diphtheria toxoid—only 6 per cent of the full dose—no toxoid sensitivity test need be done first.

Smallpox

Vaccination against smallpox is so well-established that it hardly deserves comment. There are, however, certain aspects of it which merit attention. When the infant is vaccinated at a very early age, placentally acquired antibodies from the mother may prevent a "take". Should this occur, the child should be revaccinated at about 8 months of age. It is important to vaccinate the child during the first year of life since the rare complication of encephalitis caused by the vaccinia is less likely at this time.

If the infant, or any close member of the household, has eczema or some other skin eruption, vaccination should be postponed. A generalized vaccinia can follow in such cases.

Most failures in vaccination are caused by poor vaccine since it is very sensitive to heat, even room temperatures. It must be kept at below zero temperatures. Revaccination every 5 years is recommended and also during epidemics.

Poliomyelitis

With the advent of the Salk poliomyelitis vaccine, an extremely useful product became available for protection against this disease. Poliomyelitis is not a problem in certain areas but it seems to be of

greatest magnitude in those countries where sanitary standards are the highest. In recent years, however, there have been some serious epidemics in Africa.

While poliomyelitis vaccine greatly reduces the incidence of paralytic forms of the disease, it does not appear to influence the intestinal phase of the infection. This means that the reservoir of infection is not reduced at all by its use. Such is not the case with diseases like pertussia, diphtheria, or smallpox. The implication, therefore, is clear. All persons within susceptible age groups should receive the vaccine.

Infants can have their poliomyelitis vaccine treatments started as early as age 2 months. The regimen consists of 3 injections of 1 ml. each with an interval of 4-6 weeks between the first two and an interval of at least 7 months between the second and the third. Even a single injection gives some protection for at least a year.

The need for booster injections after the basic immunization using 3 injections is not firmly established. Even so, many physicians are giving a booster injection every 1-2 years until the matter is clarified.

Progress has been made in developing a single pediatric product that will include poliomyelitis vaccine with the triple antigent already described; namely, that for diphtheria, tetanus, and pertussis. Preliminary clinical testing of such a product has been quite successful. Such combined prophylaxis would be ideally suited for pediatric practice since it requires only three injections of 0.5 ml. and yet gives protection against all four diseases.

SELECTED ABSTRACTS

Factors Influencing the Acceptance of the Salk Vaccine Program. Glasser, M. A. *Am. J. Pub. Health 48:*141 (1958). The National Foundation for Infantile Paralysis undertook a study in early 1957 to seek an answer as to the reasons for many persons not taking advantage of the availability of the Salk vaccine, even though some 43 million children and adults in the target group (all persons under 40 and pregnant women) had been vaccinated. The ultimate goal of the Foundation was 100 per cent vaccination in the target group.

The author discussed the findings of the study. It was found that a significant number of persons in the target group were still unprotected. There was little variation by regions, except a somewhat lower rate in the South, probably due to economic factors, and in the West, probably attributable to the Cutter 'incident'. Other than in the South, there was little indication that cost was a major factor in preventing vaccination. Knowledge concerning the vaccine was found to be widespread but there were some gaps in knowledge, particularly concerning the availability of the vaccine, which contributed somewhat to the incidence of nonvaccination. Doubts about the effectiveness of the vaccine and its safety seemed to have been largely dispelled. The predominant reasons for nonvaccinated adults not having taken advantage of the opportunity to be vaccinated appeared to be simple procrastination and a feeling by some that they were not susceptible to the disease. Nonvaccinated adults tended to be from low socio-economic status groups (annual income of less than $5000 and less than high school graduation) and were less likely to be able to answer questions of fact about polio and the vaccine.

The author concluded that the study showed that, by and large, people were failing to take advantage of the vaccine, not because of specific resistance to it, but because of lack of definite, positive influences which might direct them to have the inoculations. It was also concluded that the most direct method for accelerating such a vaccination program would be to stimulate informal discussion about the vaccine among people of the various socio-economic groups, to stimulate them to want to do what their friends had done.

The Flavoring of Pharmaceutical Preparations. Cook, Marvin K. *Drug and Cosm. Ind. 81:*750 (1957). The author reviewed the many aspects of the flavoring of pharmaceutical preparations in an interesting and informative manner. He pointed out that the successful flavoring of a pharmaceutical preparation is dependent upon a number of factors. Of prime importance are the painstaking selection of a flavor that is truly harmonious with the product, selecting one that is effective in masking undesirable tastes contributed by the medicinal, and the utilization of the undesirable medicinal taste as a base upon which to build a palatable formulation.

The physical attributes of a preparation, such as viscosity, texture, and color contribute markedly to flavor sensation and retention. Solvents have a marked effect upon the flavor strength and aging may strengthen or change the flavor. The addition of other substances may appreciably affect the flavor; for example, sweetness may bring a flavor to life, vanillins provide a mellow tonality to many flavors, glutamic acid may heighten a flavor, and tracts of oleo-resins, such as capsicum, may produce interesting flavor effects without being detected themselves. The author also discussed the flavoring and keeping characteristics of the most commonly employed flavoring oils. He emphasized that a trace of a contaminant, such as ragweed in a peppermint crop, may completely ruin the taste qualities of the oil. Also, oxidative products in many of the flavoring oils will make the oil unsatisfactory for use as a flavor.

In the approach to flavoring liquid preparations of pharmaceuticals which have an objectionable taste, reducing the solubility by the physical form, solvents, or by the preparation of less soluble derivatives is ofen an effective method. Flavors are still required, even with relatively insoluble drugs, and they must be selected and combined with great care. The author indicated that flavor formulation requires great skill, a large battery of samples, and much patience. He stated that there is no substitute for experience in this area of formulation. As a guide in flavoring, a series of suggested flavors were given for geriatric preparations, vitamin preparations, antacid preparations, antibiotics, oral emulsions, barbiturate preparations, sulfonamide preparations, and analgesics.

As a final warning, the author stated that the interaction of flavor and active ingredient cannot be predicted. Therefore, thorough testing to determine the stability, chemically and organoleptically, of the product must be undertaken.

Therapy With Corticotropin in Trichinosis Infestations of Children. Greenstein, N. M., and Steinberg, D. *A. M. A. J. Diseases of Children 95:261* (1958). A new approach to the treatment of trichinosis in children has been reported by the authors. They reported that an antiallergic reaction to the invading trichinae is suggested by the symptoms usually accompanying trichinosis. These symptoms include: a high eosinophil count in the blood and skeletal muscle, an urticaria-like swelling of the periorbital regions, and the presence of antibodies in the skin and blood which yield positive skin and precipitin tests and complement-fixation reactions.

Three children under twelve years of age from the same family developed trichinosis following the ingestion of homemade pork sausage. All three children were seriously ill; one, who was mentally retarded, was almost comatose. The children were given large doses of corticotropin. The response was striking, particularly in the comatose child, with a marked drop in temperature within 24 to 36 hours. The authors felt that this treatment prevented further brain damage and was, probably, life-saving for the child that had been comatose. They pointed out that cerebral symptoms from trichinosis do not usually develop unless treatment is delayed for several weeks. The case of the mentally retarded child reported was unusual in that disorientation developed within a week of the onset of other symptoms.

The author noted that one symptom, the high eosinophil count, did not respond rapidly to treatment with corticotropin but did lower slowly. However, the rapid clinical response to this therapy suggested that the allergic reaction concept to explain some of the symptoms from trichinosis may be applicable.

The Absorption of Vitamin B_{12}. Citrin, Y., DeRosa, C., and Halsted, J. A. *J. Lab. Clin. Med. 50:667* (1957). The absorption of vitamin B_{12} by the intestine was studied through urinary excretion after Co^{60}-B_{12} was administered through an intestinal or rectal tube at various locations in the small and large intestine. The subjects employed were 21 normal volunteers and 4 hospitalized patients with Addison's pernicious anemia.

The author found that 0.5 mcg. doses of vitamin B_{12} can be absorbed from the entire small intestine of normal subjects. Absorption of the vitamin from the ileum of the patients with pernicious

anemia was obtained only when intrinsic factor was added to the test dose of the vitamin. It would appear that sufficient intrinsic factor is passed through the small intestine of a normal subject to make absorption of the vitamin possible through its entire length.

Absorption of vitamin B_{12} in doses of 0.5 to 3 mcg. from the colon could not be demonstrated. Even when intrinsic factor was added to the dose or when the administration of neomycin or tetracycline preceded the test dose, absorption was not detectable from urinary excretion tests. It would appear that the colon is incapable of absorbing vitamin B_{12}. The presence of intrinsic factor did not alter the nonabsorption and the prior administration of antibiotics would appear to rule out the possibility that the vitamin was used up or bound by bacteria in the colon.

The authors also indicated that the instillation of vitamin B_{12} into the duodenum provided greater absorption than that obtained following oral administration. They suggested that the stomach may play some type of inhibitory role in the utilization and absorption of vitamin B_{12}.

The Coating of Tablets With Polyvinylpyrrolidone and Acetylated Monoglyceride. Ahsan, S. S., and Blaug, S. M. *Drug Standards 26:29* (1958). Two film-forming materials were investigated with regard to their effectiveness in the coating of tablets using conventional pan-coating equipment. An alcoholic solution of polyvinylpyrrolidone was applied to compressed tablets in four steps in a coating pan. Experimentally, 9, 6, 3, and 2 ml. volumes of the solution were applied in sequence to 500 tablets. Treatment sequence after each such addition of solution was: 2-minute rotation in pan, 2-minute rotation with warm air, 1-minute standing with warm air. The coatings were found to be uniform, smooth, and hard but brittle. Polyethylene glycol 600 was then included and the proportions varied in order to eliminate the brittleness of the coating. The formula selected as most satisfactory was: polyvinylpyrrolidone 5 per cent w/v, polyethylene glycol 600 2 per cent w/v, 70 per cent alcohol sufficient to make 100 per cent (Solution A). The coating produced with this solution was described as being uniform, smooth, hard, nontacky, nonbrittle and having an average thickness of about 0.0017 inch.

The solution was then modified to include, in addition, acetylated monoglyceride 5 per cent w/v (Solution B). The technique of application was the same except that the tablets and solution were warmed in order to insure complete solution of the acetylated monoglyceride and a uniform coat. Color coating was accomplished by dissolving or dispersing the color in the coating solution and applying it to the coated tablets. Polishing of the coated tablets was accomplished by the use of a carbon tetrachloride solution containing 150 gr. carnauba wax and 75 gr. white wax per pint.

The disintegration time of tablets coated with Solution B was 1030 sec.; for Solution A, 933 sec.; and for uncoated tablets, 953 sec. Thus, it would seem that the disintegration time was not affected appreciably by this coating. The durability of the tablets coated with Solution B was markedly superior to that of uncoated tablets. Resistance to high humidity was greatest with tablets coated with Solution B. They were unaffected by storage for 5 months at a temperature of 37° C. and 90 per cent relative humidity. Those coated with Solution A showed slight softening, while uncoated tablets showed marked softening under the same storage conditions.

The authors concluded that these film-coating materials provided an effective coating for tablets. The film did not appreciably increase the size of the tablet and it could be applied simply and quickly. The film was uniform, smooth, durable and resistant to humid storage conditions. The coating material is also noncaloric and nontoxic.

Treatment of Plantar Interdigital Fungus Infections and Intertrigo. Strauss, John S. *GP 17:*108 (1958). The author stressed the importance of distinguishing between fungus infections and intertrigo, the two most common types of interdigital disease. The signs particularly characteristic of interdigital fungus infection are scaling and involvement of more than one area of the foot, especially the sole and nails, in addition to the interdigital areas. Final confirmation should be by microscopic verification of the presence of fungi. The primary sign of intertrigo is maceration (sodden, moist, white, dead-appearing skin) with erythema.

The treatment of intertrigo involves bed rest in severe cases, exposure of the affected areas to the drying effect of air, and short soaks in mild solutions such as 1:60 Burow's solution to remove ac-

cumulated debris. No medication should be used in uncomplicated cases although a drying powder may be used to absorb excess moisture.

Several treatment programs were undertaken among a group of adult male prisoners where control could be maintained over the treatment. The mycologic cure rate was different from that of the clinical cure rate, the latter being almost always followed by a relapse after the cessation of treatment. Using wet dressings, the mycologic cure rate was 32 per cent following formalin soaks, 10 per cent after Burow's solution soaks, and 33 per cent after the use of Castellani's paint. With powders, a nonmedicated powder gave a mycologic cure rate of 9 per cent and a medicated powder (Desenex) gave a cure rate of 58 per cent. When ointments were used, a nonmedicated ointment gave a 9 per cent mycologic cure rate, Whitfield's ointment gave a 60 per cent cure rate, and a medicated ointment (Desenex) gave a cure rate of 50 per cent.

Commenting upon the treatment employed, the author stated that wet dressings and paints provided a high incidence of clinical remissions but did not show a high degree of mycologic cures. Ointments were found to be satisfactory and not prone to exacerbate lesions or increase maceration. Whitfield's ointment was found to cause contact dermatitis quite frequently.

In conclusion, the author pointed out that in spite of conscientious therapy, relapses are common, frequently from reinfection from other areas of the foot.

BOOK REVIEWS

Index of Plants of North Carolina With Reputed Medicinal Uses. Marion Lee Jacobs, Ph.D., formerly Dean and Professor of Pharmaceutical Chemistry, University of North Carolina and Henry M. Burlage, Ph.D., formerly Professor of Pharmacy, University of North Carolina and Dean and Professor of Pharmacy and Pharmaceutical Chemistry, University of Texas. 322, i-xii pages. Price $7.50 postpaid. Order from Henry M. Burlage, 702 E. 43rd St., Austin 5, Texas.

North Carolina has been and still is one of the most important crude drug producing areas in the world. This position is, no doubt, due to its geographic location and its diversified climate and topography. The latter includes the low coastal plains and savannahs, the piedmont, and a portion of the mountainous region of the Atlantic Coast states.

An introductory chapter deals with a brief history of the drug industry of the state. Almost fifteen hundred plants are listed according to families, all of which are reputed to have been used as medicines. Many of these plants are reported to have been used by various Indian tribes of the Southeastern United States as therapeutic agents. Many such uses have been included under the general heading of action and uses.

A monograph of each plant includes the botanical name, its status with regards to the official standards; i.e., the Pharmacopoeia of the United States of America and the National Formulary. Synonyms for each plant, habitats, medicinal uses including the parts and preparations employed are also included. Whenever reported in the literature, chemical constituents are indicated.

The information included in this work has been obtained from more than ninety different literary sources including herbals, manuals, etc., ranging in the dates of publication from the early years of the nineteenth century to recent periods.

Indexes of plant families, botanical nomenclature, common and generic names, constituents reported, therapeutic and other uses serve as valuable aids in locating the information. Chronological, numerical, and alphabetical author indexes of the references are included.

Trace Analysis. John H. Yoe and Henry J. Koch, Jr. xiii + 672 pp. John Wiley & Sons, Inc., New York 16, N. Y., 1957. Price $12.00.

TRACE ANALYSIS is an ambitious attempt to acquaint the biologist, physiologist, and the chemist with both the new as well as the established techniques which are available for the analysis of trace constituents of matter. It is a collection of 24 technical papers which were presented at the Symposium on Trace Analysis, held at the New York Academy of Medicine on November 2, 3, and 4, 1955. These papers, each of which was contributed by a recognized authority, are appropriately classified and placed in one of the book's major parts. Part 1, Methodology, contains 20 papers; Part 2, Instrumentation, contains 2 papers; and Part 3, Sensitivity, Separation, Concentration, and Contamination, contains 2 papers. Each chapter includes a selected list of references, and the discussion and comments which followed the presentation of the paper.

The techniques reviewed in Part 1 are: Chromatography and Electrochromatography, Ion Exchange, Extraction, Chemical Microscopy, Spot Tests, Colorimetry, Fluorometry, Flame Spectrometry, Potentiometry, Coulometry, Polarography and Voltametry, Amperometry, Emission Spectrochemical Analysis, Gamma-Ray Spectroscopy, Mass Spectroscopy, X-Ray Spectroscopy, X-Ray Micrography, Neutron Activation Analysis, and Microbiological Techniques. Although it is acknowledged that many of these techniques are applicable to the analysis of trace organic constituents, emphasis is placed on the collection, separation, and determination of inorganic ions.

Instrumentation and The Interaction of Beta Particles with Matter are the titles of the papers in Part 2. The chapter on instrumentation is concerned with the role of transducers, electronics, servomechanisms, data assimilation, and computers in present day instrumentation. A report on the reflection of beta particles and its application to trace analysis is contained in the second chapter.

Part 3 contains a necessary and enlightening discussion of the sensitivity of activation analysis as compared to that of other methods. Tables and comparison bar graphs are included. The last and indispensable chapter of this book concerns separation, concentration, and contamination; in fact, the operations which can appreciably influence the reliability of the determinations. Purification and storage of reagents, separation methods, and contamination hazards are reviewed.

This compendium of analytical techniques is recommended as an introduction to the field of trace analysis.

H. JOHNSTON

Medicinal Chemistry. Volume II. F. F. Blicke and C. M. Suter, Editors. vii + 311 pp. John Wiley & Sons, Inc., New York 16, N. Y., 1956. Price $10.00; Volume III, F. F. Blicke and R. H. Cox, Editors. vii + 346 pp. John Wiley & Sons, Inc., New York 16, N. Y., 1956. Price $10.50.

In keeping with the first volume of this series, Volumes II and III consist of chapters on specific phases of medicinal chemistry authored by well-known workers in their respective areas. Volume II deals with: Some Chemical Aspects of Cardiac Glycosides, Synthetic Estrogens, Arylpiperidines as Analgesics, and β-Haloethylamine Adrenergic Blocking Agents with their structure-activity relationships. Volume III is devoted to Methadone and related Analgesics, Quaternery Ammonium Germicides, Non-Mercurial Diuretics, and Synthetic Analogs of Physostigmine. Each chapter is adequately referenced and contains a wealth of information in the form of tables which illustrate structures of the various types of compounds investigated, with their relative activities, if known. Some synthetic data and pharmacologic test procedures are also included to aid in the evaluation of the screening methods used.

These two volumes should be in the personal library of anyone engaged in the field of medicinal chemistry or pharmacology.

A. R. GENNARO

The Chemistry of Organometallic Compounds. E. G. Rochow, D. T. Hurd and R. N. Lewis. vi + 344 pp. 1957. John Wiley and Sons, Inc., New York 16, N. Y. Price $8.50.

The authors have done well in presenting the chemistry of the organometallic compounds in a comprehensive but interesting fashion. The book is essentially divided into three sections devoted to, first, general information, theory and preparative methods, including a very enlightening chapter on the carbon-metal bond. Secondly, comprising the main portion, the compounds of the metals as they are grouped in the periodic table are discussed. Finally, two chapters are concerned with the use of organometallic compounds in organic syntheses and special compounds such as fluorocarbon derivatives, carbides, hydrides, etc. The literature appears to be covered through 1955 with some references in 1956. This book is indeed a worthwhile addition to the literature of chemistry.

A. R. GENNARO

The Chemistry of the Steroids. By W. Klyne. 216 pp. John Wiley and Sons, Inc., New York 16, N. Y., 1957. Price $3.50.

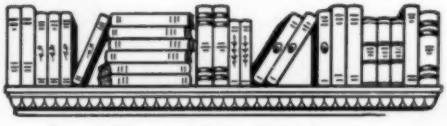
It is extremely unfortunate that a book such as this is a rarity. Dr. Klyne has accomplished something that most authors no doubt set out to do but too often fail. *The Chemistry of the Steroids* is a concise, very well-written compendium of the nomenclature, structure, reactions, and properties of the synthetic and naturally occurring steroids and related compounds. Nine chapters are devoted to stereochemistry, nomenclature, physical properties (including ultraviolet and infrared data), chemical properties of both simple and complex functional groups, naturally occurring steroids (sterols, vitamins, bile acids, estrogens, etc.), and chemical separations.

The reviewer, not being primarily interested in steroid chemistry, has often been amazed at the many complex reactions involved in the transformations, synthesis, and structure proof of so large a molecule. After spending only a few hours with this book, the whole field of steroid chemistry has been bared—not so much that any reader will

become proficient in this field—but sufficient knowledge of the subject is easily acquired to cause the reader to become quite interested and conversant in the chemistry of the steroids.

As Dr. Klyne states, "The purpose of the book is to provide an outline of the chemistry of steroids to the non-chemical reader in hopes that it will enable him to discuss his problems with the chemist better". It is the opinion of the reviewer that the author has succeeded masterfully and the book is highly recommended to the chemist, biologist, and other workers striving to keep abreast of this challenging and interesting subject.

A. R. GENNARO



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